REMARKS and ARGUMENTS

The Claims have been amended by amending Claims 1 and 4; by canceling Claims 2, 5, and 6; and by adding new Claim 55.

Claims 1, 4, 7-18, 20, 21, and 51-55 are pending in this application. Of the pending Claims, Claims 1, 7, 8, 20, 21, and 51-53 were rejected in the January 30, 2006 Office Action. Claims 4, 9-18, and 54 were objected to for reasons of form as being dependent on a rejected base Claim, but were otherwise found to be allowable in substance.

Claim 1 has been amended in its part (c), primarily to recite that *n* is from 4 to 10. Basis for the amendment to Claim 1 is found, for example, in paragraph 0034 of the specification. See particularly subpart (c) on page 13 of the specification. Concerning the amendment in numerical range, see generally M.P.E.P. 2163.05, underneath the heading "III. Range Limitations," first paragraph.

Basis for new Claim 55 is found, for example, in paragraph 0034 of the specification. See particularly subpart (c) on page 13 of the specification.

These amendments are made without prejudice to Applicants' right to pursue the canceled subject matter in one or more continuation applications.

The § 119(e) Priority Date

The Office has acknowledged that Claims 53 and 54 are entitled to the benefit of the provisional priority date, but has taken the position that the other pending Claims are not.

Applicants do not concede that the remaining Claims are not also entitled to the benefit of the provisional filing date. Applicants reserve the right to demonstrate such priority at a later date, should the need arise. However, it is respectfully submitted that it is not necessary to decide this question for the time being. With the exception of Claims 53 and 54, in the discussion below it will be assumed for the sake of argument that the Claims might only be entitled to the benefit of the later nonprovisional filing date. Even if one makes this assumption, for the reasons given below it is respectfully submitted that all grounds of rejection should be withdrawn.

Preliminary Note Concerning the Novelty of the Independent Claims

Claims 1 and 53 are the two independent Claims. If the independent Claims are novel and nonobvious, it logically follows that the dependent Claims are necessarily novel and nonobvious as well. See M.P.E.P. § 2143.03, first paragraph. Therefore, the following discussion of novelty focuses on the two independent Claims, Claims 1 and 53, discussed separately below.

The §§ 102 (a) and (b) Rejections of Independent Claim 1

Applicants do not waive any of their earlier arguments concerning novelty, and reserve the right to present those arguments anew at a later date.

It is respectfully submitted, however, that the present amendment to Claim 1 clearly distinguishes Claim 1 from each of the three printed publications cited by the Office against Claim 1.

In particular, part (c) of amended Claim 1 now includes the limitation that

> --$(S)_n$ is a hydrophilic region comprising hydrophilic amino acids or other hydrophilic groups; wherein *n* is from 4 to 10, and wherein said hydrophilic region has a size not larger than about the size of a decapeptide.--

The three references cited by the Office do not satisfy this limitation.

The *Organic Letters* Paper. The January 30, 2006 Office Action asserted that a compound disclosed in the Fu *et al. Organic Letters* paper would have anticipated Claim 1 (as Claim 1 was then written), with the value of *n* set equal to 0 (Jan. 30, 2006 Office Action, par. 4, pp. 2-3). Claim 1 as amended, however, requires that *n* must be at least 4. The cited compound from the *Organic Letters* paper does not satisfy the limitations of part (c) of amended Claim 1. The *Organic Letters* paper does not anticipate amended Claim 1.

The *Journal of Organic Chemistry* Paper. Likewise, the January 30, 2006 Office Action asserted that a compound disclosed in the Fu *et al. Journal of Organic Chemistry* paper would have anticipated Claim 1 (as Claim 1 was then written), with the value of *n* set

equal to 0 or 1 (Jan. 30, 2006 Office Action, par. 5, pp. 3-4). Because amended Claim 1 requires that *n* must be at least 4, the *Journal of Organic Chemistry* paper does not anticipate amended Claim 1.

The Fu Dissertation. The January 30, 2006 Office Action asserted that a compound disclosed in the Fu Dissertation would have anticipated Claim 1 (as Claim 1 was then written), with the value of *n* set equal to 0 or 1 (Jan. 30, 2006 Office Action, par. 6, pp. 4-5). Because amended Claim 1 requires that *n* must be at least 4, the Dissertation does not anticipate amended Claim 1.

The Aucoin Oral Presentation.

Applicants previously submitted the December 19, 2005 Affidavit of inventor Robert Hammer to show that the Aucoin oral presentation represented, at least in pertinent part, the inventors' own work, and that the presentation was therefore removed as a reference under § 102(a).

The Office has repeated the rejection that Claim 1 is anticipated by the Aucoin presentation. With all respect, the rationale for repeating this rejection is not understood. The Office is respectfully requested to withdrawn this ground of rejection, or in the alternative, to clarify the basis for the rejection so that a more responsive reply might be made.

The paragraph bridging pages 10-11 of the January 30, 2006 Office Action appears to suggest that the Hammer Affidavit did not clearly identify who were the inventors of the AMY-1 and AMY-3 peptides. The Office's attention is respectfully directed to the following excerpt from section 7 of the Hammer Affidavit:

> The sequences of AMY-1, AMY-2, and AMY-3 were conceived by Dr. McLaughlin and me. Their synthesis was conceived by Dr. Fu and me. The synthesis of the unnatural amino acid dibenzylglycine, one of the components of the AMY-1, AMY-2, and AMY-3 peptides, was conceived by Dr. Miller. To the extent that the presentation discloses these peptides and their synthesis, Dr. Aucoin learned that information directly or indirectly from these other inventors. Dr. Aucoin made the surprising discovery that AMY-2,

> for example, causes aggregation into a non-toxic, non-fibril conformation, as opposed to inhibiting all aggregation.

The quoted section directly and clearly specifies who conceived the sequence and synthesis of the AMY-1, AMY-2, and AMY-3 peptides: Drs. Hammer, McLaughlin, Fu, and Miller. The quoted section directly and clearly states that to the extent the presentation discloses the peptides and their synthesis, Dr. Aucoin, the presenter, learned that information directly or indirectly from those inventors. Dr. Aucoin himself made the surprising discovery that AMY-2, for example, causes aggregation into a non-toxic, non-fibril conformation, as opposed to inhibiting all aggregation.

The Hammer Affidavit makes clear that the Aucoin presentation was, at least in pertinent part, a presentation of the inventors' own work.

It is respectfully submitted that the December 19, 2005 Affidavit removed the Aucoin presentation as a reference, and that this ground of rejection should be withdrawn accordingly. Strictly in the alternative, the Office is respectfully requested to clarify this ground of rejection, to explain with greater specificity what the Office believes is lacking from the Hammer Affidavit, so that a more responsive reply might be made.

The § 102(a) Rejection of Claim 53

The sole ground of rejection entered against Claim 53 was that it was said to be anticipated by the *Organic Letters* paper under § 102(a).

As the January 30, 2006 Office Action effectively acknowledged (page 7), the *Organic Letters* paper may be removed as a reference against Claim 53 by showing that the paper is, at least in pertinent part, a publication of the inventors' own work. However, the January 30, 2006 Office Action said that the showing made to date had not sufficed to remove the paper as a reference.

The Office Action acknowledged, however, that the December 19, 2005 Affidavit of inventor Robert P. Hammer, particularly paragraph 5, had removed the *Organic Letters* paper as a reference against dependent Claim 54. Once the paper has been removed as a reference against dependent Claim 54, for the reasons given below it then automatically

follows that the paper has also been removed as a reference effective against independent Claim 53.

The only pertinent disclosure cited from the *Organic Letters* paper was a single species, the peptidyl compound AMY-1 (SEQ ID NO 4).

M.P.E.P. § 715.03, subpart I(B), second paragraph provides in part:

> Where the only pertinent disclosure in the reference or activity is a single species of the claimed genus, the applicant can overcome the rejection directly under 37 CFR 1.131 by showing prior possession of the species disclosed in the reference or activity.

The January 30, 2005 Office Action acknowledged, in effect, that Paragraph 5 of the Hammer Affidavit showed the inventors' possession of the AMY-1 species prior to the publication of the *Organic Letters* paper.

M.P.E.P. § 715.03, subpart I(B) provides that where the only pertinent disclosure is a single species within a claimed genus, and where the Applicants have demonstrated possession of that species prior to the publication of the reference, it then automatically follows that the reference may no longer be cited against the claimed genus.

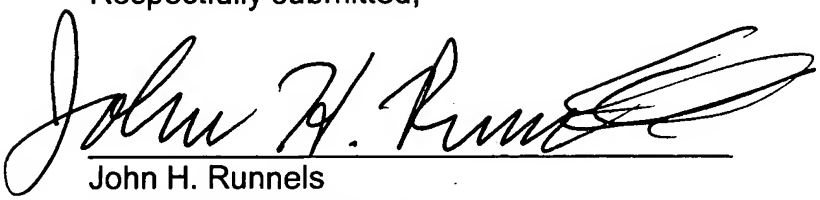
Independent Claim 53 is directed to a genus that includes the species AMY-1. As provided in M.P.E.P. § 715.03, subpart I(B), the inventors' possession of the AMY-1 peptide prior to publication of the *Organic Letters* paper removes that paper as a reference against Claim 53.

It is respectfully submitted that all prior art rejections have been overcome, or should otherwise be withdrawn.

Conclusion

Allowance of Claims 1, 4, 7-18, 20, 21, and 51-55 at an early date is respectfully requested.

Respectfully submitted,



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Appendix A. Claim Amendments.

1. (currently amended) A compound for inhibiting the toxicity of an amyloid protein or amyloid peptide, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least four modified or unmodified amino acids; said compound comprising a peptidyl sequence selected from the group consisting of:

$$X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2}\text{-}(S)_n\ ;$$

$$(S)_n\text{-}X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2};$$

$$Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}(S)_n\ ;$$

$$(S)_n\text{-}Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\ ;$$

$$X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2}\text{-}X_{aa3}\text{-}(S)_n\ ;$$

$$(S)_n\text{-}X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2}\text{-}X_{aa3}\ ;$$

$$Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}Y_{AA3}\text{-}(S)_n\ ;$$

$$(S)_n\text{-}Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}Y_{AA3}\ ;$$

$$(S)_n\text{-}X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2}\text{-}X_{aa3}\text{-}Y_{AA3}\ ;$$

$$Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}Y_{AA3}\text{-}X_{aa3}\text{-}(S)_n\ ;$$ and

$$(S)_n\text{-}Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}Y_{AA3}\text{-}X_{aa3}\ ;$$

wherein:

(a) X_{aa1}, X_{aa2}, and X_{aa3} are natural or synthetic amino acids that are identical or homologous to alternating amino acids of the aggregation-inducing sequence of the amyloid protein or amyloid peptide, and that have side chains adapted for cross-strand side chain interactions with a β-sheet;

(b) Y_{AA1}, Y_{AA2}, and Y_{AA3} are natural or synthetic amino acids that are identical or homologous to alternating amino acids of the aggregation-inducing sequence of the amyloid protein or amyloid peptide; wherein Y_{AA1}, Y_{AA2}, and Y_{AA3} correspond to amino acids that will be positioned on opposite faces of a β-sheet containing the amino acids that correspond to X_{aa1}, X_{aa2}, and X_{aa3}; and wherein the amino acids in the amyloid protein or amyloid peptide that correspond to X_{aa1}, X_{aa2}, and X_{aa3} alternate with the amino acids in the amyloid protein or amyloid peptide that correspond to Y_{AA1}, Y_{AA2}, and Y_{AA3}; wherein at least two of Y_{AA1}, Y_{AA2}, and Y_{AA3} are $C^{\alpha,\alpha}$-disubstituted amino acids;

(c) $(S)_n$ is a hydrophilic region comprising hydrophilic amino acids or other hydrophilic groups; wherein ~~$(S)_n$ consists of from 0 to 10 amino acids or otherwise,~~ *n* is from 4 to 10, and wherein said hydrophilic region has a size not larger than about the size of a decapeptide;

(d) either or both ends of said peptidyl sequence optionally comprise additional functionality that does not adversely affect the compound's ability to inhibit the toxicity of an amyloid protein or amyloid peptide, as compared to an otherwise identical compound lacking such additional functionality; and

(e) the number of amino acids in the aggregation sequence of the amyloid protein or amyloid peptide may be the same as, or different from, the number of natural or synthetic amino acids in said peptidyl sequence.

2 - 3. (canceled).

4. (currently amended) The compound of Claim [[2,]] 1, wherein said compound is $(Lys)_7$-Dibg-Val-Dbzg-Phe-Dpg-NH_2 (SEQ ID NO: 5).

5 - 6. (canceled)

7. (original) The compound of Claim 1, wherein the aggregation-inducing sequence is selected from the group consisting of KLVFFA (SEQ ID NO: 3); FLVHS (SEQ ID NO: 9); NFLVH (SEQ ID NO: 10); NFGAIL (SEQ ID NO: 11); VGGAVVTGV (SEQ ID NO: 12); VNITIKQHTVTTTT (SEQ ID NO: 13); LANFLV (SEQ ID NO: 14); FLVHSS (SEQ ID NO: 15); AGDV (SEQ ID NO: 16); and Q_m; wherein *m* is an integer from 25 to 45.

8. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is KLVFFA (SEQ ID NO: 3).

9. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is FLVHS (SEQ ID NO: 9).

10. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is NFLVH (SEQ ID NO: 10).

11. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is NFGAIL (SEQ ID NO: 11).

12. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is VGGAVVTGV (SEQ ID NO: 12).

13. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is GAV.

14. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is VNITIKQHTVTTTT (SEQ ID NO: 13).

15. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is LANFLV (SEQ ID NO: 14).

16. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is FLVHSS (SEQ ID NO: 15).

17. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is AGDV (SEQ ID NO: 16).

18. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is Q_m; wherein *m* is an integer from 25 to 45.

19. (canceled)

20. (original) The compound of Claim 1, wherein each of $Y_{AA1,}$ Y_{AA2}, and Y_{AA3} is an $C^{\alpha,\alpha}$-disubstituted amino acids.

21. (original) A composition of matter comprising the compound of Claim 1, and a pharmaceutically acceptable carrier.

22 - 50 (canceled)

51. (previously presented) A compound as recited in Claim 1, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least six modified or unmodified amino acids, and wherein said peptidyl sequence is selected from the group consisting of:

$(S)_n$-X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3}-Y_{AA3} ;

Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}- X_{aa3}-$(S)_n$; and

$(S)_n$-Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}- X_{aa3} .

52. (previously presented) A compound as recited in Claim 1, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least five modified or unmodified amino acids, and wherein said peptidyl sequence is selected from the group consisting of:

X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3}-$(S)_n$;

$(S)_n$-X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3} ;

Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}-$(S)_n$; and

$(S)_n$-Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3} .

53. (previously presented) A compound comprising a peptidyl sequence selected from the group consisting of:

$$X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2}\text{-}X_{aa3}\text{-}Y_{AA3}\text{-}(S)_n\ ;$$

$$(S)_n\text{-}X_{aa1}\text{-}Y_{AA1}\text{-}X_{aa2}\text{-}Y_{AA2}\text{-}X_{aa3}\text{-}Y_{AA3}\ ;$$

$$Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}Y_{AA3}\text{-}\ X_{aa3}\text{-}(S)_n\ ;$$ and

$$(S)_n\text{-}Y_{AA1}\text{-}X_{aa1}\text{-}Y_{AA2}\text{-}X_{aa2}\text{-}Y_{AA3}\text{-}\ X_{aa3}\ ;$$

wherein:

(a) X_{aa1} is L-lysine or D-lysine, X_{aa2} is L-valine or D-valine, and X_{aa3} is L-phenylalanine or D-phenylalanine;

(b) Y_{AA1} is a $C^{\alpha,\alpha}$-disubstituted amino acid analog of leucine, Y_{AA2} is a $C^{\alpha,\alpha}$-disubstituted amino acid analog of phenylalanine, and Y_{AA3} is a $C^{\alpha,\alpha}$-disubstituted amino acid analog of alanine; and

(c) $(S)_n$ is a hydrophilic region comprising hydrophilic amino acids or other hydrophilic groups.

54. (previously presented) The compound of Claim 53, wherein said compound is Lys-Dibg-Val-Dbzg-Phe-Dpg-$(Lys)_6$-NH_2 (SEQ ID NO: 4).

55. (new) The compound of Claim 1, wherein *n* is from 4 to 6.